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Hepatoid Adenocarcinoma of the Stomach – a rare histology of Gastric Adenocarcinoma in an adolescent: a case report.

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Abstract

Hepatoid adenocarcinoma is a rare subtype of extra-hepatic adenocarcinoma generally characterized by hepatocellular carcinoma like foci in the background of adenocarcinoma. Stomach is the most frequent site where hepatoid adenocarcinoma occurs, although it has been described in many other organs. We describe a case of 16 years old adolescent girl who was diagnosed as a case of "hepatoid adenocarcinoma of stomach', an unlikely presentation at this young age.

Keywords: Hepatoid adenocarcinoma, stomach, adolescent.

1. Introduction:

Gastric adenocarcinoma is a malignant epithelial tumor, originating from glandular epithelium of the gastric mucosa. Hepatoid adenocarcinoma (HAC) is a type of extra-hepatic adenocarcinoma, which shows a striking morphologic similarity to hepatocellular carcinoma (Gao *et al*. 2007). It is generally characterized by adenocarcinomatous and hepatocellular carcinoma (HCC)-like foci. This variant of adenocarcinoma has been demonstrated to be an alpha-fetoprotein (AFP)-producing carcinoma arising in extra hepatic organs, and it mimics hepatocellular carcinoma in morphological and functional terms. Alpha-fetoprotein (AFP) is a fetal serum protein produced by fetal liver and yolk sac cells, and by some fetal gastrointestinal cells. After birth, the levels of the protein in serum rapidly decrease.

2. Case report:

A 16 years old adolescent girl presented with aggravating abdominal pain for 2 months. She had history of repeated vomiting, aggravated by food intake for last three months, and anorexia, fatigue and unexplained weight loss of ten kilograms over the same duration. The initial ultrasonography was unremarkable with no focal defects seen in liver or abdominal lymphadenopathy. The upper gastrointestinal endoscopy revealed a circumferential mass lesion at the gastric antrum occluding the lumen. The biopsies from the antral growth showed histological features of fragmented bits of ulcero-necrotic slough, granulation tissue and acute inflammatory exudates invaded by several atypical cells with pleomorphic hyperchromatic nuclei, irregular nuclear membrane and prominent nucleoli; features highly suggestive of a poorly differentiated malignant lesion. Tumor marker (CEA and CA19-9) serum levels were normal. Based on this report the patient underwent a distal gastrectomy with dissection of sixteen lymph nodes and biopsy of omental tissue. The stomach showed a large tumour of nine centimeters in its greatest axis, with histology showing features of "polygonal cells arranged in solid nest, with scattered large multinucleated giant cells, and well differentiated papillary pattern with clear cytoplasm – suggestive of Hepatoid Adenocarcinoma". [Figure 1] The carcinoma had infiltrated the muscle coat and had extended into the serosa. The surgical lines of resection were free of lesion. Four out of sixteen lymph nodes were positive for metastasis. The omental tissue did not show any metastasis. The tumour was immunopositive for cytokeratin and Alpha-fetoprotein (AFP) [Figure 2] and negative for C-kit, CD 34, Desmin, SMA and S-100 protein. The postoperative AFP was elevated measuring 5090ng/ml. A post-operative CT scan showed multiple liver metastases in both

lobes with more on right lobe and portal lymphadenopathy. The patient underwent palliative chemotherapy of six cycles comprising of docetaxel, cisplatin and 5fluorouracil.

3. Discussion:

Stomach cancer is the fourth most common cancer worldwide with 930,000 cases diagnosed in 2002 (Parkin *et al*. 2005). The studies show that less than 5% of stomach cancers occur in people less than 40 years of age with 81.1% of that 5% in the age-group of 30 to 39 and 18.9% in the age-group of 20 to 29 (Simsa *et al*. 2004). The overwhelming pathological variety of gastric carcinoma is adenocarcinoma found in 90% of cases.

Ishikura *et al.* proposed the term "hepatoid adenocarcinoma of the stomach" for primary gastric carcinomas characterized histologically by hepatoid differentiation and the production of large amounts of AFP (Ishikura *et al*. 1985). This unique histological hepatoid adenocarcinoma has also been reported in the lung, pancreas, uterus and ovary (Okunaka *et al*. 1992; Yamada et al. 1994; Itoh *et al*. 1992; McIntire *et al*. 1975). The tumor is immunohistochemistry positive is for cytokeratin and Alpha fetoprotein and negative for C-kit, CD 34, Desmin, SMA and S-100 protein.

There has been mention of case reports of "hepatoid adenocarcinoma of the stomach" in the literature. In the literature, 86 cases described by the term "hepatoid adenocarcinoma of the stomach" have been reported, including the present case. In 2001, *Inawaga et al* revised all these cases and published a report with the main clinical characteristics of this pathological variety (Inagawa *et al*. 2001). The average age of the patients was 63.5 years (range, 44–87 years), and the male-to-female ratio was 58:25 (the sex was not stated for 2 patients). In most of these patients, the tumors occurred mainly at the antrum (60.2%). The average serum AFP level was 51130.1 ng/ml (range, less than 1.0–700000ng/ml); that is, much higher than normal. Although there were no major symptoms sufficient to allow diagnosis of this type of cancer, epigastric pain and general fatigue because of anemia, were the most common symptoms. The average maximal tumor diameter was 6.5cm (range, 1.6–14.0cm). Most cases also had metastatic disease to the lymph nodes or liver.

Furthermore, most of the patients died within 2 years of surgery, despite systemic chemotherapy having been administered in several patients. These reports suggest that even early stage hepatoid adenocarcinoma has an extremely poor prognosis, because of the frequent occurrence of liver and/or lymph node metastases (Nagai *et al*. 1993; Chang *et al*. 1991). However, the reasons for the poor prognosis are not clearly understood. *Nagai et al.* reported that hepatoid adenocarcinoma had a poor prognosis compared with that for AFP-producing non-hepatoid adenocarcinoma (Nagai *et al*. 1993). One possibility is that hepatoid adenocarcinoma produces AAT and/or ACT as well as AFP. AAT and ACT have immunosuppressive and protease-inhibiting properties that enhance invasiveness [Redelman & Hudig 1980; Pasternack & Eisen 1985). Also, AFP has a suppressive effect on lymphocyte transformation. In addition, *Koide et al*. have reported that AFP-producing gastric cancer has high proliferative activity, weak apoptosis, and rich neovascularization (Koide *et al*. 1999). Furthermore, as *Chang et al.* have reported, even if no metastasis is present preoperatively, liver metastasis can occur within a year after surgery, and, thus, close observation and long-term follow-up of patients are required (Chang *et al*. 1991).

The management of this special subtype has still not clearly been demarcated with majority of patients detected in metastatic stage requiring palliative chemotherapy with docetaxel, doxorubicin, cisplatin, capecitabine, irinotecan and 5-fluorouracil in various combinations (Van Cutsem *et al*. 2006; Dank *et al*. 2008). The outcome of the subtype is poor for all stages of disease.

In conclusion, we report a rare case of hepatoid adenocarcinoma of the stomach, diagnosed in an adolescent patient with well defined clinicopathological features. The only hope for curative treatment in this rare variety of tumour is early diagnosis and administration of novel chemotherapeutic drugs for better disease control.

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Figures:

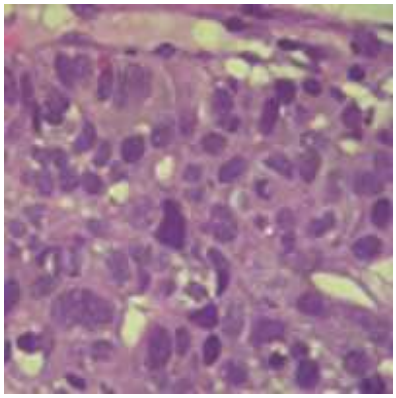

Figure 1. Gastric biopsy of the distal gastrectomy specimen 400x hematoxylin eosin staining

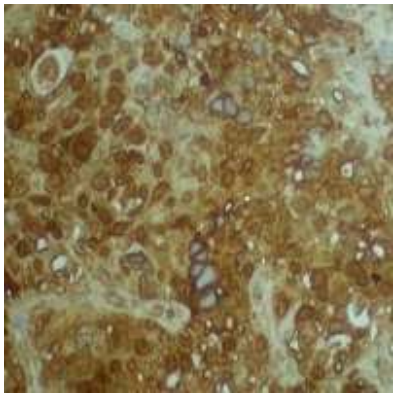

Figure 2. The gastric biopsy was strongly immnuopositive for AFP